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Imperforate Anus in Feingold Syndrome

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A father and daughter had the characteristic findings of Feingold syndrome including microcephaly, short palpebral fissures, brachydactyly with clinodactyly of fifth fingers, and bilateral syndactyly of second to third and fourth to fifth toes. The infant presented with long-gap esophageal atresia without fistula (type A). Her father, who had short stature and learning disabilities, had congenital imperforate anus with a recto-vesical fistula. This is the first report of distal intestinal atresia in Feingold syndrome. Am. J. Med. Genet. 92:166–169, 2000.

KEY WORDS: esophageal atresia; duodenal atresia; syndactyly; microcephaly; brachydactyly

INTRODUCTION

The clinical phenotype of Feingold syndrome, first reported in 1975 [Feingold, 1975] was more completely delineated in recent publications [Courtans et al., 1997; Feingold et al., 1997]. Feingold syndrome, also known as MODED (microcephaly-oculo-digito-esophageal-duodenal) syndrome [Frydman et al., 1997] is a clinically variable autosomal dominant disorder comprising hand and foot abnormalities, microcephaly, short palpebral fissures, learning disabilities, and esophageal and/or duodenal atresia. Esophageal atresia with or without tracheo-esophageal fistula occurs in around 30% of described individuals, sometimes in combination with duodenal atresia or obstruction.

We describe a family with Feingold syndrome, ascertained through an infant with esophageal atresia and minor anomalies. The infant's affected father was born with imperforate anus and recto-vesical fistula, a previously unreported anomaly in individuals with Feingold syndrome.

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CLINICAL REPORT
Patient 1 (III-3)

The proposita (Fig. 1) was the first child of a 19-year-old woman and the third child of her 43-year-old partner (Fig. 2); there was no consanguinity. Both parents had a history of learning disability. Fetal sonography at 18 weeks of gestation demonstrated polyhydramnios and an absent stomach bubble, suggesting esophageal atresia. The amniocyte karyotype was normal. The infant was born at term by vaginal delivery with forceps assistance under general anesthesia; her birth weight was 2,325g (<10th centile), head circumference (OFC) 32 cm (10th centile), and length 48.5 cm (50–90th centile). She had short palpebral fissures, brachydactyly with clinodactyly of the fifth fingers (Fig. 3), and bilateral syndactyly of second to third and fourth to fifth toes (Figs. 4 and 5). Passage of a naso-gastric tube was unsuccessful, and investigations confirmed a wide-gap esophageal atresia without fistula (type A). The chest film showed only 11 pairs of ribs. Echocardiogram documented a small ventricular septal defect and a

Fig. 1. III-3, lateral view of face.

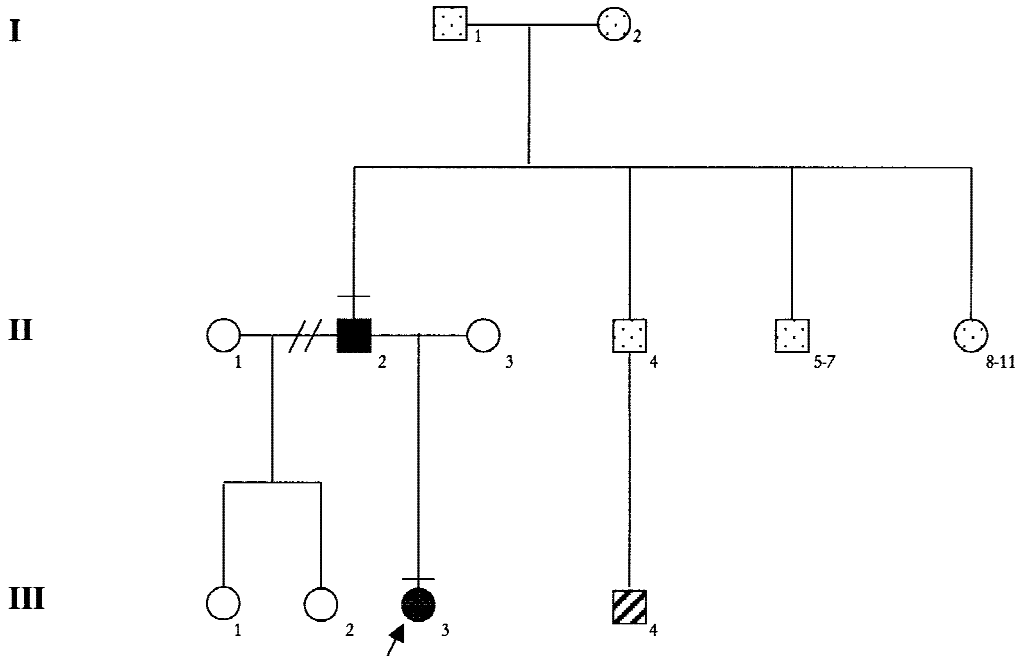

Fig. 2. Pedigree of the family: ● affected, ▨, "esophageal blockage" no further details available; ⊡, no information could be obtained.

persistent foramen ovale. Renal ultrasonography demonstrated small normal kidneys (left 3.0, right 3.2 cm). A G-banded karyotype was normal, 46,XX at 500-band resolution. Gastrostomy and insertion of a feeding tube was performed at age 6 days and cervical esophagostomy at age 8 weeks. At age 12 weeks, on discharge from hospital her weight was 4,800 g (25–50th centile) and head circumference 36.1 cm (<10th centile). Her behavior and development was normal for her age.

Patient 2 (II-2)

The baby's father was born with imperforate anus with rectovesical fistula, diagnosed at age 9 days and managed with a colostomy. Later, he was noted to have microcephaly, fifth finger clinodactyly, and developmental delay. Closure of the colostomy could not be maintained, despite several attempts in childhood, because of persistent problems with constipation, fecal incontinence, and rectal prolapse. On examination he had short stature, microcephaly (head circumference 51 cm; < 3rd centile), prominent nose, brachydactyly with bilateral fifth finger clinodactyly, hypoplastic distal creases of the fourth and fifth fingers, and minimal 2–3 and moderate 4–5 syndactyly of toes bilaterally.

The father could not provide any clear information about his family, but recalled that his brother (II-4) had a child (III-4) with a "swallowing blockage" in the newborn period. We were unable to contact any other family members or trace their medical records.

Fig. 3. III-3, right hand showing brachydactyly and clinodactyly.

DISCUSSION

In 1975, Feingold reported on a syndrome of microcephaly, facial and hand anomalies, tracheo-esopha-

Fig. 4. III-3, left foot showing syndactyly of toes 2–3 and 4–5.

geal fistula, duodenal atresia, and developmental delay [Feingold, 1975]; later he reported on a second family [Feingold, 1978]. Since then 15 families with Feingold syndrome have been reported [König et al., 1990; Brunner and Winter, 1991; Hall, 1994; Courtans et al., 1997; Feingold et al., 1997; Frydman et al., 1997]. This autosomal dominant disorder is also known as MODED (microcephaly-oculo-digito-esophageal-duodenal) syndrome [Frydman et al., 1997]. The disorder exhibits marked intrafamilial variability, particularly with regard to gastrointestinal manifestations, but a review [Feingold et al., 1997] suggested that all have hand anomalies, 80–90% have foot abnormalities, 87.5–100% have microcephaly, and 52–90% have learning disability.

The hand and foot anomalies are distinctive. Frydman et al. [1997] concluded that they best resemble brachydactyly type A4 (MIM *112800; short or absent middle phalanges of the second and fifth fingers, lack of middle phalanges of the 2nd-5th toes) [Frydman et al., 1997] with addition of varying degrees of cutaneous syndactyly of the 2nd–3rd and 4th–5th toes, and a wide gap between the first and second toes [Brunner and Winter, 1991]. In addition to microcephaly there are facial similarities including narrow palpebral fissures, relatively prominent nose, and mild retrognathia. Upper gastrointestinal anomalies are present in up to one-half of reported cases [Courtans et al., 1997; Feingold et al., 1997]. The commonest gastrointestinal anomaly is tracheo-esophageal fistula or tracheal atresia, present in at least 25% of patients, and duodenal atresia or obstruction, present in over 20% [Feingold et al., 1997]. This may represent a biased estimate as many of the published families were ascertained through an index case with intestinal atresia.

The family we report includes at least two individuals with Feingold syndrome, the proposita and her father, both with microcephaly, short palpebral fissures, brachydactyly with clinodactyly of the fifth fingers, and bilateral partial 2–3 and 4–5 syndactyly of the toes; the father also has learning disability and short stature. The daughter had esophageal atresia without fistula (esophageal atresia type A) while the father had imperforate anus with recto-vesical fistula.

We were unable to find any other previously reported patient with Feingold syndrome and imperforate anus. Although the combination could be coincidental, it seems more likely to be an uncommon manifestation of the disorder. There is a non-random association of ano-

Fig. 5. III-3, right foot showing deep plantar creases and syndactyly of toes 4–5.

rectal agenesis +/± urorectal fistula and esophageal atresia +/± esophageal fistula, either as a dyad or as components of sporadic multiple congenital anomaly associations (e.g., VATER association) [Botto et al, 1997], or chromosomal disorders (e.g., duodenal atresia and imperforate anus in Down syndrome). Multiple intestinal atresias at any level, from stomach to anus [Dallaire and Perreault, 1974; MIM #243150] is reported as an autosomal recessive trait, and is postulated to have a vascular basis. The association of intestinal atresia with syndactyly in Feingold syndrome suggests the possible involvement of a developmental gene involved in the regulation of apoptosis.

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